Abstract:

Glucose lowering effects of a single dose GW671021B at 100 mg/kg in fed Western Diet C57BL/6J mice +/- STZ

WD + STZ + Vehicle  -  -  -  -  -  -  WD + STZ + GW021B
WD + Vehicle

Time (hours)

0  1  2  3  4  5  6

-150 -100 -50  0  50  100


Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(U))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(H(i))
- if inventorship (Rule 4.17(iv))

Published:

- with international search report

Date of publication of the international search report:

12 July 2007

For two-letter codes and other abbreviations, refer to the "Guide Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Title: GENES ASSOCIATED WITH TYPE II DIABETES MELLITUS
**INTERNATIONAL SEARCH REPORT**

International application No
PCT/US2006/033564

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, Sequence Search, WPI Data, EMBASE, BIOSIS, INSPEC, FSTA, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>A</td>
<td>TORRES S H ET AL: &quot;Inflammation and nitric oxide production in skeletal muscle of type 2 diabetic patients&quot; JOURNAL OF ENDOCRINOLOGY, vol. 181, no. 3, June 2004 (2004-06), pages 419-427, XP002416277 ISSN: 0022-0795 Relevant for non unity abstract figure 2 page 424, column 1, paragraph 3 page 425, column 2, paragraph 2 - page 426, column 1, paragraph 1</td>
<td>1</td>
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</table>

X Further documents are listed in the continuation of Box C. X See patent family annex

* Special categories of cited documents *

'A' document defining the general state of the art which is not considered to be of particular relevance

'E' earlier document but published on or after the international filing date

'L' document which may throw doubts on probity daim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

'O' document referring to an oral disclosure, use, exhibition or other means

'P' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

'Z' document member of the same patent family

Date of the actual completion of the international search 24 January 2007

Date of mailing of the international search report 19/04/2007

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentillaan 2 NL - 2280 HV RUISWINK Tel. (+31-70) 340-2040, Tx. 31 651 epc nl, Fax: (+31-70) 340-3016

Authorized officer

VAN DER KOOIJ, M

Form PCT/ISA/210 (second sheet) (April 2005)
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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<tr>
<td>A</td>
<td>KUMARAMANI KAVEL G ET AL: &quot;Inducible nitric oxide synthase gene and diabetic retinopathy in Asian Indian patients&quot; CLINICAL GENETICS, vol. 61, no. 5, May 2002 (2002-05), pages 344-348, XP002416278 ISSN: 0009-9163 Relevant for non unity abstract page 346, column 2, paragraph 2 - page 347, column 2, paragraph 2</td>
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<td>A</td>
<td>WO 99/47497 A2 (MERCK FROSST CANADA INC [CA]; GAREAU YVES [CA]; LABELLE MARC [CA]; JUT) 23 September 1999 (1999-09-23) claims 1-28</td>
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<td>F,X</td>
<td>WO 2006/017171 A (METABOLEX INC [US]; MOODIE SHONNA A [US]; ZHANG FANG [US]; RACK PAUL G) 16 February 2006 (2006-02-16) page 83, line 1 - page 85, line 2 sequences 84,86,88 claims 1,2,4-9</td>
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Continuation of Box II.1

Although claims 3-6 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box 11.2

Claims Nos.:

The present claims 3-6 encompass compounds defined only by their desired function, contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. The fact that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed, except for the compound disclosed in the description, see page 30. Undue experimentation would be required to screen compounds randomly. This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search for claims 3-6. The search of claims 3-6 was consequently restricted to compound GW671021 (see page 30).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.
INTERNATIONAL SEARCH REPORT

Box II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons.

1. ✔ Claims Nos - because they relate to subject matter not required to be searched by this Authority, namely
   Although claims 3-6 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ✔ Claims Nos - because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically.
   see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos., because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows.

see additional sheet

1. ✔ As all required additional search fees were timely paid by the applicant, this International Search Report covers all

2. ✔ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos..

4. ✔ No required additional search fees were timely paid by the applicant Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.
   1 (partially), 2-6

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 (partially), 2-6


2. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing inducible Nitric Oxide Synthase (iNOS) as screening target.

3. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing BRAF as screening target.

4. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing Caspase 8 as screening target.

5. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing Integrin Alpha 9 (ITGA9) as screening target.

6. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing A Disintegrin-like And Metalloprotease domain with Thrombospondin motifs 7 (ADAMTS7) as screening target.

7. Claim: 1 (partially)

   A method of screening for small compounds for use in treating Type II Diabetes mellitus employing Amyloid Precursor Protein as screening target.
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<th>Patent family member(s)</th>
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<td>WO 2004074514 A2</td>
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<td>CA 2516371 A1</td>
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